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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,147	03/24/2005	Martin J. Oliver	57767US005	6332

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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 12/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/510,147	OLIVER ET AL.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/5/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-15 are pending.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim 15 is objected to because of the following informalities: claim 15 does not end in a period. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 12 are vague and indefinite because these claim a "physiologically functional derivative" of formoterol, which is defined in [0029] of the specification as, "chemical

derivative of formoterol having the same physiological function as the free compound, for example, by being convertible in the body thereto." The specification in [0029] also gives esters as an example of said derivative. However, the definition in the specification is inadequate because it is based upon the function of the genus of compounds in question and does not specify what chemical moieties are required for a formoterol derivative to be "physiologically functional." Examples of compounds adhering to Applicants' definition do not cure the indefiniteness of Applicants' definition. Therefore, an ordinary skilled artisan would be unable to ascertain the metes and bounds of the term "physiologically functional derivative" as used in the claims to refer to formoterol compounds without having to rely on undue experimentation.

Claim 15 is vague and indefinite because it requires the step of (ii) dispersing particles of formoterol and some unknown pharmaceutically acceptable something, presumably a compound or compounds. A skilled artisan would be unable to ascertain the metes and bounds of this claim because the identity of the particulate pharmaceutically acceptable something dispersed along with formoterol is ambiguous. Appropriate correction and clarification are required.

The remaining claims are rejected for depending from a rejected claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue; and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9, 13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over McNamara (WO 99/65464; IDS reference) in view of Oliver et al. (U.S. Patent No. 6,120,752) ("Oliver") and Oliver et al. (U.S. Patent No. 6,054,488) ("Oliver-488").

Applicant Claims

Applicants claim (1) a pharmaceutical formulation comprising (i) particulate suspended formoterol or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof, (ii) a dissolved compound of formula (I) (e.g. ciclesonide), and (iii) a propellant selected from 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane, and a mixture thereof; (2) a

dispenser comprising an aerosol vial equipped with a dispensing valve containing a formulation according to claim 1; and (3) a method of preparing a formulation according to claim 1 comprising (i) providing a solution of the compound of formula (I) in 1,1,1,2-tetrafluoroethane and/or 1,1,1,2,3,3,3-heptafluoropropane and (ii) dispersing particles of formoterol or a pharmaceutically acceptable "something" (claim 15).

NOTE: The method of making a formulation of claim 1 (i.e. claim 15) is missing part of step (ii) as described above in the rejections under 35 U.S.C. §112, 2nd paragraph. Although this claim is indefinite, in favor of compact prosecution, the Examiner has assumed that the missing language from step (ii) is "salt, solvate, or physiologically functional derivative thereof."

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

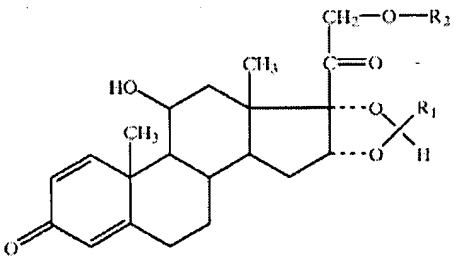
McNamara teaches pharmaceutical aerosol formulations comprising at least two or more active substances for administration by inhalation or by nasal route via propellant-driven metered dose aerosols using a fluorohydrocarbon propellant, which contains a combination of active substances, **wherein at least one active substance is present in dissolved form together with at least one other active substance in the form of suspended particles** (title, abstract, pg. 1, lines 8-10; pg. 3, lines 25-35). The propellants utilized in these formulations are particularly **TG 134a (i.e. 1,1,1,2-tetrafluoroethane) and/or TG 227 (i.e. 1,1,1,2,3,3,3-heptafluoropropane)** (pg. 3, lines 30-35). In a preferred embodiment the suspended active includes salbutamol (also known as albuterol, which is a known betamimetic/beta adrenergic agonist) and the dissolved active includes beclomethasone (an anti-inflammatory steroid). In another embodiment the suspended particles are stabilized by the addition of surfactant substances or other suspension

stabilizing agents to ensure that the suspended active particles will maintain a pharmaceutically acceptable particle size preferably not exceeding 10 microns, so that upon inhalation the active particles are small enough to penetrate deeply into the lungs (pg. 5, lines 13-25). Preferred surfactant compounds include oleic acid and sorbitan mono-, di-, or trioleates (pg. 5, line 36 through pg. 6, line 1). The amount of surfactant utilized may be an amount up to 1:1 by weight of the suspended active substances (pg.6, lines 8-12). The solubility of at least one active substance can be enhanced by the addition of one or more cosolvents (e.g. **ethanol**) in **amounts from 0.0001-50% w/w** based upon the total weight of the formulation (pg. 6, lines 29-36), wherein sufficient alcohol is present to dissolve the active substance which has to be dissolved (pg. 6, line 35 through pg. 7, line 2).

Oliver teaches:

[57] **ABSTRACT**

A pharmaceutical aerosol formulation suitable for oral and/or nasal inhalation including an anti-inflammatory steroid of the formula



in which:

R_1 is 1-butyl, 2-butyl, cyclohexyl or phenyl and

R_2 is acetyl or isobutanoyl, in particular ciclesonide. The formulations also include hydrofluorocarbon propellants such as HFC 134a and/or 227, and cosolvent such as ethanol in an amount sufficient to solubilize the ciclesonide or related steroid (and various optional ingredients, such as surfactant). The formulations exhibit very desirable physical and chemical stability, as well as excellent delivery characteristics.

Oliver teaches that ciclesonide is considered useful in inhaler formulations based upon anti-asthmatic and pharmacokinetic studies and that it has systemic activity that is three times lower than that of budesonide (i.e. systemic side effects are three times lower), but higher anti-inflammatory activity than budesonide (col. 1, lines 42-45 and 49-51). Ciclesonide can be very beneficially formulated as a physically and chemically stable solution in formulations containing hydrofluorocarbon propellants (col. 2, lines 25-29). Oliver's formulations generally contain **3-25% w/w ethanol** (col. 2, lines 56-58). The propellant in Oliver's formulations includes propellant 134a **(i.e. 1,1,1,2-tetrafluoroethane),** propellant 227 **(i.e. 1,1,1,2,3,3,3-heptafluoropropane), or a mixture thereof** (col. 2, lines 59-62). The formulations may contain surfactant (col. 2, lines 63-65). The formulations may be prepared by **adding the required amount of drug into an aerosol vial, crimping on a valve on the vial, and introducing a premixed blend of propellant and ethanol through the vial, and placed into a bath for sonication to ensure solubilization. The preferred vial material is aluminum**. The dispensing valve of the vial is a metered dose-dispensing valve (e.g. 50 microliter valve) (col. 3, lines 1-17). Specific formulations comprising ciclesonide, hydrofluorocarbon propellant, and ethanol in varying amounts are exemplified (Examples 1-16; col. 5, line 25 through col. 8, line 26). Oliver teaches that the formulations **may include additional active ingredients** (col. 8, lines 29-33).

Oliver-488 teaches pharmaceutical suspension aerosol suspension formulations suitable for aerosol administration comprising from **0.0025-0.1% w/w micronized formoterol or an acid addition salt thereof**, from **0.1-5.0% w/w ethanol**, **HFA 134a, HFA 227, or a mixture of HFA 134a and HFA 227, and optionally a surfactant**, wherein the formulation is

characterized by exhibiting no substantial growth in particle size or change in crystal morphology of the drug over a prolonged period (title abstract). **Formoterol fumarate** is a long acting beta-2 agonist developed for delivery to the respiratory system by a metered dose inhaler (MDI), which is highly potent and requires a considerably lower dosage than other drugs (col. 2, lines 50-55). Stable suspension formulations may be obtained by incorporation of micronized **bulking agent**, which will sediment in the propellant (e.g. lactose, DL-alanine, ascorbic acid, glucose, and D-(+)-trehalose dehydrate) **in an amount by weight relative to drug in the range 1:3 to 1:100** (col. 3, lines 52-61). Surfactant, such as oleic acid, can be used in amounts of 0.002-0.01% w/w (col. 4,lines 7-14). It is important that formoterol fumarate does not come into contact with high concentrations of ethanol (e.g. above 10% w/w) since this would lead to drug dissolution, formulation instability, and crystal growth problems (col. 4, lines 21-26). Oliver-488 teaches a method of making pharmaceutical formoterol fumarate suspension aerosol formulations comprising division of the ingredients into those for making the concentrate and those for inclusion in the bulk, which **includes dispersion of drug in a small quantity of propellant** (col. 4, lines 30-53; Examples 16-22: col. 7, lines 1-57). Formoterol fumarate formulations are exemplified in Examples 1-33 (col. 5, line 1 through col. 10, line 23).

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

McNamara lacks the teaching of pharmaceutical aerosol formulations comprising ciclesonide in solution (i.e. a dissolved compound of Applicants' formula (I)) in combination

with suspended particulate formoterol. These deficiencies are cured by the teachings of Oliver and Oliver-488.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of McNamara, Oliver, and Oliver-488, because McNamara teaches pharmaceutical aerosol formulations comprising two or more active agents in admixture with hydrofluorocarbon propellant and ethanol cosolvent, wherein at least one active is dissolved (e.g. beclomethasone) and at least one active ingredient is in suspension (e.g. albuterol) and both Oliver and Oliver-488 similarly teach pharmaceutical aerosol formulations comprising hydrofluorocarbon propellants and ethanol cosolvent. An ordinary skilled artisan would have been motivated to modify the teachings of McNamara to utilize ciclesonide as the dissolved drug, because it exhibits greater anti-inflammatory properties than other inhalable steroids (e.g. budesonide) and significantly decreased systemic side effects (Oliver) and has been demonstrated to form physically and chemically stable solution formulations in compositions comprising hydrofluorocarbon propellants. An ordinary skilled artisan would have been motivated to utilize formoterol fumarate as the suspended active ingredient in McNamara's formulations because it is a highly potent long acting beta-2 agonist developed for delivery to the respiratory system from a metered dose inhaler and thus can be used in much lower dosages (Oliver-488). Furthermore, it would have been obvious to a person of ordinary skill in the art to utilize the combination of a dissolved steroid and a suspended beta-2 agonist, because McNamara teaches this combination. An ordinary skilled artisan would have had a reasonable

expectation of success upon combination of the prior art references and modification of McNamara's compositions to obtain compositions comprising dissolved ciclesonide and suspended particulate formoterol, because McNamara teaches formulations comprising at least one dissolved active, at least one suspended particulate active, hydrofluorocarbon propellant, and ethanol cosolvent and the secondary prior art references teach how to obtain physically and chemically stable formulations comprising dissolved ciclesonide and suspended particulate formoterol fumarate.

In paragraph [0014] of the instant specification, Applicants' asserted that it was surprising to obtain physically and chemically stable formulations comprising formoterol fumarate in suspension, ciclesonide in solution, and HFA 134a and/or HFA 227 propellant. The Examiner has considered Applicants' data presented in the specification examples on pages 16-22, especially with regard to Applicants' assertion of surprising results. It is the Examiner's position that contrary to Applicants' assertion this result is not surprising, because the conditions needed to separately obtain physically and chemically stable (1) solutions of ciclesonide in HFA 134a and/or HFA 227 propellant and (2) formoterol fumarate suspensions in HFA 134a and/or HFA 227 propellant were known in the prior art (Oliver and Oliver-488). Furthermore, formulations comprising a dissolved steroid, a suspended betamimetic, and HFA 134a and/or HFA 227 propellant were known in the art (McNamara). Notwithstanding the unsurprising nature of Applicants' observations, even if it were surprising to obtain physically and chemically stable formulations comprising formoterol fumarate in suspension, ciclesonide in solution, and HFA 134a and/or HFA 227 propellant, Applicants' data is not commensurate in scope with what is claimed. Applicants' data (see Example 2) is limited to formulations wherein the dissolved

compound of formula (I) is ciclesonide (0.3362 % w/w); the formoterol compound is formoterol fumarate (0.0101% w/w), and also comprising lactose monohydrate (bulking agent; 0.1009 % w/w), oleic acid (surfactant; 0.0050% w/w), ethanol (5.000% w/w), and propellant 134a (94.5478 % w/w). If Applicants' data demonstrates unexpected results (the Examiner does not believe it does), it can only support this assertion for formulations comprising the components in the amounts set forth in Example 2 and cannot support this assertion for formulations lacking surfactant and/or bulking agent, comprising other formoterol compounds, and comprising other compounds of formula (I) that are not ciclesonide.

For the reasons set forth above, the Examiner concludes that claims 1-9, 13, and 15 would have been *prima facie* obvious to a person of ordinary skill in the art cognizant of the teachings of McNamara, Oliver, Oliver-488, because combination of the prior art teachings would have yielded compositions that were the same or substantially similar to what Applicants are claiming.

Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over McNamara (WO 99/65464; IDS reference) in view of Oliver et al. (U.S. Patent No. 6,120,752) ("Oliver") and Oliver et al. (U.S. Patent No. 6,054,488) ("Oliver-488") as applied to claims 1-9, 13, and 15 above, and further in view of Jinks et al. (WO 02/30394).

Applicant Claims

Applicants claim a pharmaceutical formulation comprising (i) particulate suspended formoterol or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative

thereof, (ii) a dissolved compound of formula (I) (e.g. ciclesonide), (iii) a propellant selected from 1,1,1,2-tetrafluoroethane, 1,1,1,2,3,3,3-heptafluoropropane, and a mixture thereof, and further comprising (iv) a bulking agent having a mass median diameter (MMD) of less than 1 micron.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of McNamara, Oliver, and Oliver-488 have been set forth above in the instant office action. Jinks teaches the use of particulate **bulking agents preferably having a MMD of less than 300 nm** in pharmaceutical aerosol formulations comprising a suspension of drug particles in propellant, wherein the bulking agents include ascorbic acid, saccharides, polysaccharides, amine acids, organic and inorganic salts, urea, and propliodone (abstract). Jinks has found that one can obtain improved suspension aerosol formulations by introducing a bulking agent having a MMD of less than one micron, wherein said bulking agent improves the stability of suspended drug particles, which may be micronized or other drug particles having a MMD equal to or greater than 1 microns (pg. 4, lines 15-24). Preferred bulking agents include lactose and are taught on page 6, lines 1-9. The **weight ratio of drug to bulking agent is generally in the range 1:0.1 to 1:100** (pg. 6, lines 11-13). Jinks' invention is particularly applicable to drugs formulated at a concentration less than 0.1% w/w (pg. 6, lines 15-17). The invented aerosol formulations may contain ethanol in an amount in the range 0.1-5% w/w (pg. 9, lines 1-3). Compositions comprising **formoterol fumarate** are exemplified in Examples 2 (pg. 10, line 20 through pg. 11, line 17), 5 (pg. 12, line 14 through pg. 13, line 16), and 9-12 (pg. 16, line 3 through pg. 17, line 7).

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

McNamara, Oliver, and Oliver-488 lack the teaching of composition further comprising bulking agents having a MMD less than 1 micron. This deficiency is cured by the teachings of Jinks.

Finding of Prima Facie Obviousness Rational and Motivation
(MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of McNamara, Oliver, Oliver-488, and Jinks because Jinks teaches that the incorporation of bulking agents having a MMD less than 1 micron yield improved suspension formulations, especially wherein the suspended drug is formulated at a concentration less than 0.1% w/w. An ordinary skilled artisan would have been motivated to modify the combined teachings of McNamara, Oliver, and Oliver-488 obtain with the teachings of Jinks to incorporate bulking agents having a MMD < 1 micron, because the inclusion of said bulking agents yields improves the stability of suspension formulations. A person of ordinary skill in the art would have had a reasonable expectation of success upon modification of the combined teachings of McNamara/Oliver/Oliver-488 to utilize bulking agents having a MMD < 1 micron, because Jinks' data demonstrated that incorporation of said bulking agents in suspension formulations comprising suspended formoterol fumarate improved the formulation stability (e.g. improved uniformity of the delivered dose). The Examiner's position regarding Applicants' data and assertion of surprising results is the same and is reiterated in this rejection (see the previous rejection under 35 U.S.C. §103(a)).

For the reasons set forth above, the Examiner concludes that claims 10-12 would have been *prima facie* obvious to a person of ordinary skill in the art cognizant of the teachings of McNamara, Oliver, Oliver-488, and Jinks because combination of the prior art teachings would have yielded compositions that were the same or substantially similar to what is claimed by Applicants.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over McNamara (WO 99/65464; IDS reference) in view of Oliver et al. (U.S. Patent No. 6,120,752) ("Oliver") and Oliver et al. (U.S. Patent No. 6,054,488) ("Oliver-488") as applied to claims 1-9, 13, and 15 above, and further in view of Ashurst (U.S. Patent No. 6,131,566).

Applicant Claims

Applicants claim a dispenser comprising an aerosol vial equipped with a dispensing valve containing a formulation according to claim 1, wherein an interior surface of the aerosol vial is coated with a coating comprising a fluorocarbon polymer.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of McNamara, Oliver, and Oliver-488 have been set forth above in the instant office action. Ashurst teaches **a metered dose inhaler having all or part of its internal surfaces coated with one or more fluorocarbon polymers**, optionally a blend of one or more fluorocarbon polymers in combination with one or more non-fluorocarbon polymers for dispensing an inhalation drug formulation (abstract, title). Ashurst teaches that some drugs

adhere to the inner surfaces (i.e. walls of the can, valves, and caps of the MDI), which can result in patients getting significantly less than the prescribed amount of drug upon each activation of the MDI. This problem is especially acute with hydrofluoroalkane systems (e.g. P134a and P227) (col. 1, lines 51-58). Coating the interior can surfaces of MDI's with a fluorocarbon polymer significantly reduces or essentially eliminates the problem of adhesion or deposition of albuterol on the can walls and thus ensures consistent delivery of medication in aerosol from the MDI (col. 1, lines 59-63). Suitable fluorocarbon polymers include polymers which are made of multiples of one or more of the following monomeric units: tetrafluoroethylene, (TFE; which is used to prepare **polytetrafluoroethylene** (PTFE)) perfluorinated ethylene propylene, (FEP; which is **perfluorinated ethylene propylene copolymer**, which is a copolymer of TFE and hexafluoropropylene (HFP)), pefluoroalkoxyalkylene (PFA; which is a **perfluoroalkoxy fluorocarbon polymer** which is prepared using a perfluoroalkyl vinyl ether monomer) ethylene terafluoroethylene, (**ETFE; ethylene-tetrafluoroethylene copolymer**), vinylidene fluoride (**PVDF; polyvinylidene fluoride**) and chlorinated ethylene tetrafluoroethylene (a copolymer made by copolymerizing chlorinated ethylene and tetrafluorethylene). Fluorinated polymers, which have a relatively high ratio of fluorine to carbon, such as perfluorocarbon polymers, e.g., **PTFE, PFA, and FEP are preferred** (col. 4, line 53 through col. 5, line 3).

Ascertainment of the Difference Between Scope the Prior Art and the Claims

(MPEP §2141.012)

McNamara, Oliver, and Oliver-488 lack the teaching of an aerosol vial wherein an interior surface of the aerosol vial is coated with a coating comprising a fluorocarbon polymer. This deficiency is cured by the teachings of Ashurst.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of McNamara, Oliver, Oliver-488, and Ashurst because the adhesion and/or deposition of particulate drug to the interior surfaces of an MDI or other pharmaceutical aerosol dispenser is a recognized problem in the field, especially wherein the propellant system comprises a hydrofluoroalkane (e.g. HFA 134a and/or HFA 227). An ordinary skilled artisan would have been motivated to combine the teachings of McNamara/Oliver/Oliver-488 and Ashurst, because Ashurst teaches that coating the interior can surfaces of MDI's with a fluorocarbon polymer significantly reduces or essentially eliminates the problem of adhesion or deposition of particulate drug. A person of ordinary skill in the art at the time of the instant invention would have had a reasonable expectation of success upon combination of the teachings of Ashurst with those of the combined teachings of McNamara/Oliver/Oliver-488, because Ashurst has demonstrated that the coating of a fluorocarbon polymer to the interior can surfaces of a MDI reduces and/or eliminates the problem of particulate albuterol adhesion/deposition, which is a significant problem encountered in pharmaceutical aerosol suspension formulations comprising a hydrofluorocarbon propellant system. An ordinary skilled artisan would have had a reasonable expectation that the problem of adhesion/deposition of other suspended particulate drugs in pharmaceutical aerosol formulations

comprising a hydrofluorocarbon propellant would similarly be solved by the solution invented by Ashurst, because highly fluorinated polymers are known to be used in a variety of "no-stick" (i.e. no or minimal adhesion) applications (e.g. TEFLON®-coatings). The Examiner's position regarding Applicants' data and assertion of surprising results is the same and is reiterated in this rejection (see the rejection under 35 U.S.C. §103(a) over the combination of McNamara, Oliver, and Oliver-488). It is noted that Applicants' data is limited to formulations stored in and dispensed from aluminum cans coated with fluorinated ethylene propylene (FEP) polymer.

For the reasons set forth above, the Examiner concludes that claim 14 would have been *prima facie* obvious to a person of ordinary skill in the art cognizant of the teachings of McNamara, Oliver, Oliver-488, and Ashurst because combination of the prior art teachings would have yielded an aerosol vial having interior surfaces coated with fluoropolymers that would be expected to minimize or essentially eliminate the problem of particulate drug adhesion/deposition onto the interior surfaces of said vial.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Oliver et al. (U.S. Patent No. 6,264,923) is considered pertinent because it discloses pharmaceutical aerosol solution formulations comprising ciclesonide, HFA propellant, and ethanol cosolvent.

Claims 1-15 are rejected. Claim 15 is objected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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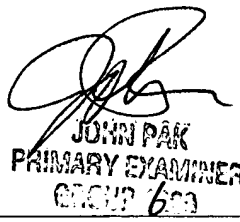

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